

REMARKS

This application is amended in a manner to place it in condition for allowance at the time of the next Official Action.

**Status of the Claims**

Claims 1-4, 6-10, 14, 15, 20, 22 and 23 are amended. Support for the substantive amendments to the claims may be found, for example, page 16, lines 19-25, the Examples section, and discussed relative to the Figures.

Claims 24 and 25 are new and are directed to features previously recited in claims 8 and 20, respectively.

Claims 5, 11-13 and 17 have been cancelled without prejudice to focus examination on transgenic mice.

Claims 1-4, 6-10, 14-16, and 18-25 remain in this application.

Claims 6, 10, 16, 18 and 21 have been withdrawn for being directed to non-elected subject matter.

**Claim Rejections-35 USC §112**

Claims 1-4, 7-9, 11-15, 19, 20, 22 and 23 were rejected under 35 U.S.C. §112, first paragraph, for not complying with the enablement requirement.

The Official Action stated that, relative to the elected subject matter, the specification is enabling for a

transgenic mouse. Accordingly, the elected claims are direct to a transgenic mouse, and claims 11-13 are cancelled.

Therefore the elected claims are believed to enabled by the specification, and withdrawal of the rejection is respectfully requested.

Claims 14-23 were rejected under 35 U.S.C. §112, second paragraph, for being indefinite.

Specifically, these claims were rejected for omitting steps. Accordingly, claims 14, 22 and 23 were amended in a manner suggested by the Official Action and described in the Examples.

Therefore, withdrawal of the rejection is respectfully requested.

#### **Claim Rejections-35 USC §103**

Claims 1-4, 7-9, 11-15, 19, 20, 22 and 23 were rejected under 35 U.S.C. §103(a) as being unpatentable over CHISTI et al. 2001 (CHISTI) in view of NILSBERTH et al. 2001 (NILSBERTH). This rejection is respectfully traversed for the reasons below.

The position of the Official Action was that it would have been obvious to the ordinary artisan to modify the teachings of CHISTI by substituting a DNA sequence encoding APP-Arctic for either APP-717 or APP-Swe to produce a transgenic mouse expressing a DNA sequence encoding APP-Arctic and a second APP-FAD mutation to determine the mechanism of APP-Arctic pathology.

However, the Official Action does not define the level of ordinary skill in the art, i.e. inquiry (C) according to MPEP 2141, in a manner consistent with the claimed subject matter and the cited documents.

Applicants respectfully direct the Examiner's attention to the first sentences of the discussion section of CHISTI beginning at page 21567.

*Although transgenesis is generally regarded as a routine technique, the APP gene first cloned over a decade ago, can be seen to present particular challenges. Difficulties encountered thus far include low expression levels in first generation Tg mice, neonatal lethality associated with high level expression in second generation mice, and physiological endoproteolysis to generate multiple subfragments with diverse biological activities, some of which [...] may confound the study of neuropathogenesis.*

Applicants also respectfully direct the Examiner's attention to the paragraph spanning pages 21562-21563, where the problems with existing animal models of AD are discussed.

In view of these passages, it is clear that CHISTI and coworkers, who must be considered as skilled artisans, did not consider it obvious that simply any mutation could be introduced into the APP gene predictably resulting in a useful animal model.

Thus, the person of ordinary skill in the art would not have found it obvious to combine the teachings of CHISTI and NILSBERTH, and reasonably expect to successfully arrive at the subject matter of the claimed invention.

On the contrary, CHISTI appears to discourage one of ordinary skill in the art to make such a modification. On page 21569 col. 2 lines 41-43, CHISTI suggests that the disclosed animal model is a useful and validated system. In this art, it is essential to have a validated system, the characteristics of which are well-known and reliable. The fact that CHISTI mentions that the system discussed in the document was validated, in combination with the fact of the great uncertainty of APP transgenic technology, one of ordinary skill in the art would have been discouraged from further modifying the system, as such further modification of a validated system would lead to unpredictable results.

The Official Action cites the holdings of KSR, e.g., rationales A, B, E, F and G in support of the modification of CHISTI.

However, the KSR exemplary rationales A, B, E and F all require that the invention is in some way predictable from the combination of prior art references. However, as discussed above, the field of APP-transgenic animal models is considered unpredictable by the skilled person. Thus, these rationales are not applicable and fail to support a finding of obviousness.

Moreover, the KSR rationale G requires a teaching, suggestion or motivation in the prior art to modify the prior art. For the reasons discussed above, CHISTI implicitly, if not explicitly, teaches that the animal model used should not be

further modified. Thus, CHISTI teaches away from modification, and, fails to suggest even approaching the claimed invention.

Therefore, the proposed combination fails to render obvious claims 1-4, 7-9, 11-15, 19, 20, 22-25, and withdrawal of the rejection is respectfully requested.

### **Conclusion**

In view of the amendment to the claims and the foregoing remarks, the present application is in condition for allowance at the time of the next Official Action. Withdrawal of the rejections and allowance on that basis is respectfully requested.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON

/Robert A. Madsen/  
Robert A. Madsen, Reg. No. 58,543  
209 Madison Street, Suite 500  
Alexandria, VA 22314  
Telephone (703) 521-2297  
Telefax (703) 685-0573  
(703) 979-4709

RAM/jr